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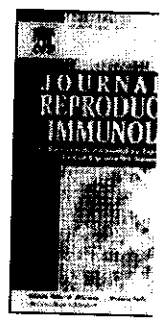

Topic 10: Mechanisms, diagnosis and treatment of immune-mediated abortions

10.1 (O)

Cytokine gene polymorphisms in women with recurrent spontaneous abortion

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Background: In recurrent spontaneous abortion (RSA) defective production of TH2-type cytokines (such as IL-10) and higher production of TH1-type cytokines (such as TNF-α) have been reported. Furthermore, single nucleotide polymorphisms in non-coding regions of cytokine genes are associated with differential ability of cytokine production. The importance of these bi-allelic polymorphisms in several infectious and autoimmune diseases has been investigated.

Objective: To analyze the prevalence of bi-allelic polymorphisms in TNF-α (G −308 A), TNF-β (G +252 A), IL-4 (C −590 T) and IL-10 (C −592 A) genes in RSA patients relative to healthy women.

Methods: 54 women with RSA and 110 normal women with at least three successful pregnancies were included in this study. The −308 G-to-A polymorphism in TNF-α promoter region were checked by allele specific PCR (ASPCR) and bi-allelic polymorphisms in three other cytokine genes were determined by PCR-RFLP method.

Results: No significant differences in the distribution of TNF-α, TNF-β and IL-4 alleles were observed in RSA patients compared with controls, but in the case of IL-10 the frequency of −592*C allele were 90% in RSA patients compared with 72% in control group ($P \leq 0.005$).

Discussion: Data of this preliminary work indicate that IL-10 gene polymorphisms can be considered as a genetic factor for susceptibility to RSA in Iranian women. The study of other allelic polymorphisms in IL-10 promoter gene (−819, −1082) or investigation of other cytokine gene polymorphisms is suggested.

10.2 (O)

TGF-β1 gene polymorphism (position −509 C/T) in repeated spontaneous abortion (RSA)

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Repeated spontaneous abortion is regarded as a common pregnancy complication in southern Iran. The exact cause of RSA has not yet been known. Increases in serum level of autoantibodies, serum lipid levels and change in serum level of proinflammatory cytokines have been reported in RSA cases. TGF-β1 is produced by TH2 lymphocytes and plays an important role in the physiology of pregnancy. Elevated serum level of this cytokine in RSA has already been reported. In this investigation, the change at position −509 of TGF-β1 was studied in 114 RSA and 74 normal female subjects from southern Iran by PCR-RFLP. Results indicate that 45 (39.1%) of RSA and 18 (24.3%) of normal subjects were homozygote CC at this position. In addition 47 (40.9%) of cases and 45 (60.8%) of normal individuals were heterozygote CT. 23 (20%) of 114 and 11 (14.9%) of 74 normal individuals were homozygote TT. The results indicate that there is a statistically significant difference between heterozygote RSA cases and those of normal female individuals. The importance of higher frequency of hetrozygocity among normal subjects in comparison with RSA will be discussed.